CLAIMS

1. A method for typing a target gene, which method comprises:

a) isolating a target cell comprising a target gene from a suitable sample and obtaining a preparation comprising a target nucleotide sequence that is at least a part of said target gene from said isolated target cell and, optionally another nucleotide sequence not related to said target gene;

b) providing a chip comprising a support suitable for use in nucleic acid hybridization having immobilized thereon an oligonucleotide probe complementary to said target nucleotide sequence and at least one of the following oligonucleotide control probes: a positive control probe, a negative control probe, a hybridization control probe and an immobilization control probe; and

c) hybridizing said preparation obtained in step a) to said chip provided in step b) and assessing hybridization between said target nucleotide sequence and/or said another nucleotide sequence and said probes comprised on said chip to determine the type of said target gene.

2. The method of claim 1, wherein the target cell is a leukocyte, but not limited to leukocye.

3. The method of claim 1, wherein the target gene is a human leukocyte antigen (HLA). This method also can be used for the genetic typing of other genes.

4. The method of claim 1, wherein the suitable sample is is selected from the group consisting of blood, saliva, hair, a human tissue that comprises a huamn nucleic acid, and any other human tissues containing nuclear cells.

5. The method of claim 4, wherein the blood sample is selected from the group consisting of serum, plasma and whole blood.

6. The method of claim 5, wherein the blood sample is fresh or low-temperature conserved whole blood.

7. The method of claim 1, wherein the target cell is isolated from the suitable sample using a magnetic microbead.

8. The method of claim 7, wherein the magnetic microbead has a diameter ranging from about 5 μm to about 200 μm.

9. The method of claim 1, wherein the preparation of the target nucleotide sequence comprises a nucleic acid amplification step.

10. The method of claim 9, wherein the target nucleotide sequence is obtained via nucleic acid amplification directly from the isolated target cell.

11. The method of claim 9, wherein the target nucleotide sequence is obtained via nucleic acid amplification using a nucleic acid template isolated from the isolated target cell.

12. The method of claim 9, wherein the nucleic acid amplification step is selected from the group consisting of polymerase chain reaction (PCR), ligase chain reaction (LCR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA) and transcription-medicated amplification (TMA).

13. The method of claim 12, wherein the TMA is driven by a T7 promoter.

14. The method of claim 12, wherein the PCR is asymmetrical PCR.

15. The method of claim 14, wherein the two primers used in the asymmetrical PCR have a ratio ranging from about 1:5 to about 1:200.

16. The method of claim 14, wherein the two primers used in the asymmetrical PCR have same or different Tm values.

17. The method of claim 14, wherein the difference between the Tm value of the two primers used in the asymmetrical PCR ranges from about 1°C to about 20°C.

18. The method of claim 14, wherein three primers are used in the asymmetrical PCR, two of the primers having same of similar Tm value and the difference between the Tm value of the two primers and that of the third primer ranges from about 1°C to about 20°C.

19. The method of claim 14, wherein the primers are straight-chain primers or comprise a hairpin structure.

20. The method of claim 12, wherein a single or multiple annealing temperatures are used in the PCR.

21. The method of claim 20, wherein the difference between the annealing temperatures ranges from about 1°C to about 20°C.

22. The method of claim 1, wherein the target nucleotide sequence obtained in step a) is single-stranded DNA or RNA.

23. The method of claim 22, wherein the single-stranded DNA or RNA is positive or negative strand.

24. The method of claim 1, wherein a labeled target nucleotide sequence is obtained in step a).

25. The method of claim 24, wherein the labeled target nucleotide sequence comprises a fluorescent or biotin label.

26. The method of claim 1, wherein the another nucleotide sequence is complementary to the positive control probe, the negative control probe or the hybridization control probe comprised on the chip.

27. The method of claim 1, wherein the probes comprised on the chip are positive-stranded or negative-stranded probes.

28. The method of claim 1, wherein the probes comprised on the chip are modified.

29. The method of claim 28, wherein the probe modification is selected from the group consisting of 5'-NH_2 modification, 5'-SH modification, 5'-polyT(or A, C or G) modification, 5'-biotin modification, 3'-NH_2 modification, 3'-SH modification, 3'-polyT(or A, C or G) modification and 3'-biotin modification.

30. The method of claim 1, wherein the chip comprises 1-400 different types of probes.

31. The method of claim 1, wherein the chip comprises multiple arrays of probes and each array comprises 1-400 different types of probes.

32. The method of claim 1, wherein the probes are immobilized on the chip at a temperature ranging from about 37°C to about 100°C.

33. The method of claim 1, wherein the chip is modified.

34. The method of claim 33, wherein the chip modification is selected from the group consisting of CHO, NH_2, poly-lysine, SH, BSA, Streptavidin, agarose gel and Polyacrylamide gel modification.

35. The method of claim 1, wherein the sequence, purity or terminal modification of the probes is assessed.

36. The method of claim 35, wherein the sequence, purity or terminal modification of the probes is assessed via DHPLC.

37. The method of claim 1, wherein multiple copies of a probe is immobilized on the chip.

38. The method of claim 1, wherein 1-10 copies of a probe is immobilized on the chip.

39. The method of claim 1, wherein the multiple copies of a probe are immobilized adjacently or separately on the chip.

40. The method of claim 39, wherein the multiple copies of a positive control probe are immobilized on the chip and the variations in the length and sequence of the immobilized positive control probes, when hybridized with the target nucleotide sequence or the another nucleotide sequence in the preparation provided in step a), create a group of hybridization signals having strong-to-weak or weak-to-strong orderly magnitude.

41. The method of claim 1, wherein the positive control probe is complementary to a portion of the target nucleotide sequence, a nucleotide sequence amplified synchronically with the target nucleotide sequence or a synthetic nucleotide sequence.

42. The method of claim 41, wherein the negative control probe has about 1-3 basepair mismatches when compared to the positive control probe.

43. The method of claim 1, wherein the hybridization control probe is complementary to a synthetic nucleotide sequence not related to the target gene.

44. The method of claim 43, wherein the hybridization control probe is complementary to a synthetic labeled nucleotide sequence or has about 1-2 basepair mismatches when compared to the synthetic labeled nucleotide sequence.

45. The method of claim 1, wherein the immobilization control probe does not generate any hybridization signal.

46. The method of claim 1, wherein one end of the immobilization control probe is chemically modified and the other end of the immobilization control probe has a detectable label.

47. The method of claim 1, wherein the chip comprises a positive control probe, a negative control probe, a hybridization control probe and an immobilization control probe.

48. The method of claim 1, wherein the positive control probe, the negative control probe, the hybridization control probe and the immobilization control probe are immobilized on the four corners of the chip, in the center of the chip or have any suitable orderly or random immobilization pattern.

49. The method of claim 1, wherein the hybridization reaction in step c) is conducted in a hybridization solution comprising sodium chloride/sodium citrate (SSC) and a surfactant.

50. The method of claim 49, wherein the hybridization solution comprises from about 3X to about 10X SSC.

51. The method of claim 49, wherein the surfactant has a concentration ranging from about 0.05% (w/w) to about 5% (w/w).

52. The method of claim 49, wherein the surfactant is selected from the group consisting of sodium dodecyl sulfate (SDS), Triton 100 and sodium lauryl sarcosine (SLS).

53. The method of claim 1, wherein the hybridization reaction in step c) is conducted at a temperature ranging from about 42°C to about 70°C.

54. The method of claim 1, further comprising a washing step after the hybridization reaction.

55. The method of claim 54, wherein the washing step is conducted in a washing solution comprising a surfactant having a concentration ranging from about 0.% (w/w) to about 2% (w/w).

56. The method of claim 54, wherein the washing step is conducted for a time ranging from about 5 minutes to about 30 minutes.

57. The method of claim 1, wherein the immobilization efficiency is assessed by analyzing a signal from the immobilization control probe.

58. The method of claim 1, wherein the overall hybridization efficiency is assessed by analyzing the hybridization between the hybridization control probe and a labeled synthetic nucleotide sequence not related to the target gene.

59. The method of claim 1, wherein the hybridization specificity is assessed by analyzing the ratio between the hybridization signal involving the positive control probe and the hybridization signal involving the negative control probe, and the ratio between the hybridization signal involving the positive hybridization control probe and the hybridization signal involving the negative hybridization control probe, and increased ratios indicating the increased hybridization specificity.

60. The method of claim 1, wherein, in hybridizations involving a group of closely related probes, a positive signal(s) is determined based on the follwing criteria:

a) the ratio of the hybridization signal over backbround noise is more than 3;

b) the ratio of the hybridization signal over a relavent positive control probe hybridization signal is within a pretermined range;

c) compairing hybridization signals of all probes giving positive signals based on the steps of a) and b), or hybridization signals of two probes giving two strongest hybridization signals when only one probe giving positive signal based on the steps of a) and b), to determine whether the signal is positive or negative; and

d) there are 2 or less than 2 positive signals involving the group of closely related probes.

61. The method of claim 1, wherein the oligonucleotide probe is complementary to a target HLA gene.

62. The method of claim 61, wherein the oligonucleotide probe comprises a nucleotide sequence that:

a) hybridizes, under high stringency, with a target HLA nucleotide sequence, or a complementary strand thereof, that is set forth in Table 1; or

b) has at least 90% identity to a target HLA nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is set forth in Table 1.

63. The method of claim 61, wherein the oligonucleotide probe comprises a nucleotide sequence, or a complementary strand thereof, that is set forth in Table 1.

64. The method of claim 61, wherein the chip comprises all nucleotide sequences, or a complementary strand thereof, that are set forth in Table 1.

65. An oligonucleotide probe for typing a HLA target gene comprising a nucleotide sequence that:

a) hybridizes, under high stringency, with a target HLA nucleotide sequence, or a complementary strand thereof, that is set forth in Table 1; or

b) has at least 90% identity to a target HLA nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is set forth in Table 1.

66. The probe of claim 65, which comprises DNA, RNA, PNA or a derivative thereof.

67. The probe of claim 65, which comprises a nucleotide sequence, or a complementary strand thereof, that is set forth in Table 1.

68. The probe of claim 65, which is labeled.

69. The probe of claim 68, wherein the label is selected from the group consisting of a chemical, an enzymatic, an immunogenic, a radioactive, a fluorescent, a luminescent and a FRET label.

70. An array of oligonucleotide probes immobilized on a support for typing a HLA target gene, which array comprises a support suitable for use in nucleic acid hybridization having immobilized thereon a plurality of oligonucleotide probes, at least one of said probes comprising a nucleotide sequence that:

a) hybridizes, under high stringency, with a target HLA nucleotide sequence, or a complementary strand thereof, that is set forth in Table 1; or

b) has at least 90% identity to a target HLA nucleotide sequence comprising a nucleotide sequence, or a complementary strand thereof, that is set forth in Table 1.

71. The array of claim 70, wherein the plurality of probes comprise DNA, RNA, PNA or a derivative thereof.

72. The array of claim 70, wherein at least one of the probes comprises a nucleotide sequence, or a complementary strand thereof, that is set forth in Table 1.

73. The array of claim 70, which comprises all of the probes comprising the nucleotide sequences, or a complementary strand thereof, that are set forth in Table 1.

74. The array of claim 73, wherein at least one of the probes is labeled.

75. The array of claim 74, wherein the label is selected from the group consisting of a chemical, an enzymatic, an immunogenic, a radioactive, a fluorescent, a luminescent and a FRET label.

76. The array of claim 70, wherein the support comprises a surface that is selected from the group consisting of a silicon, a plastic, a glass, a ceramic, a rubber, and a polymer surface.